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Hepatitis B Vaccine: Evidence Confirming Lack of AIDS Transmission

Recent studies have provided important additional assurances concerning the safety of hepatitis B (HB) vaccine. The vaccine currently licensed in the United States is produced from pooled plasma of hepatitis B surface antigen-positive individuals, some of whom are also in high-risk groups for acquired immunodeficiency syndrome (AIDS). Concern has been expressed that the etiologic agent of AIDS might be present in the vaccine and survive the inactivation steps used in the manufacturing procedure. The concerns persisted, despite the fact that these steps were reportedly able to inactivate representative members of all known virus groups. The recent identification of a retrovirus as the etiologic agent of AIDS has allowed workers to (1) directly test the inactivation of the AIDS virus by the inactivation steps used in the vaccine manufacturing procedure; (2) look for the AIDS virus' nucleic acid sequences in the vaccine; and (3) look for serologic markers of infection from the AIDS virus in vaccine recipients. Concurrently, monitoring of AIDS patients and high-risk groups has continued in order to look for any epidemiologic evidence of an association between HB vaccine and AIDS.

The effect of the HB vaccine inactivation process on the AIDS virus and two other human retroviruses (HTLV-I and HTLV-II) was studied. Three separate inactivation steps are used in the manufacture of the U.S.-licensed HB vaccine: (1) 1 μg/ml pepsin, pH 2, 37 C (98.6 F), 18 hours; (2) 8 molar urea, 37 C (98.6 F), 4 hours; and (3) 0.01% formaldehyde, 37 C (98.6 F), 72 hours. In separate studies conducted between CDC and the vaccine manufacturer Merck, Sharp & Dohme (MSD), and between State University of New York (SUNY) Upstate Medical Center and MSD, cell culture supernatant fluid containing the AIDS virus and cultured cells containing HTLV-I, HTLV-II, and the AIDS virus were transported to MSD and individually exposed to the three inactivation steps. The materials were then returned to CDC and SUNY for detection of residual viral infectivity. Virus infectivity was assayed by adding the treated material to cultured lymphocytes and periodically monitoring these for signs of viral replication (reverse transcriptase activity and virus antigen expression) (*1*) and in the case of HTLV-I and HTLV-II, transformation (*2,3*). No residual virus was detected in material treated with formalin or urea, while material treated with pepsin at pH 2 did have residual virus present. Heat, an inactivation step used in vaccines manufactured outside the United States, has also been shown to inactivate the AIDS virus (*4*).

The second approach, which attempted to detect AIDS virus-related nucleic acid sequences using dot blot hybridization analysis of the vaccine with an AIDS virus deoxyribonucleic acid (DNA) probe, was done at MSD using as a positive control infected cellular (ribonucleic acid) RNA preparations provided by CDC. The vaccine contained no detectable AIDS virus-related sequences at a sensitivity of less than one picogram of DNA per 20-μg dose of vaccine.

The third approach attempted to detect seroconversion to AIDS virus antibodies in paired sera of HB vaccine recipients. Paired sera were examined at CDC using a highly sensitive and specific ELISA assay for the AIDS virus. No seroconversions were detected in 19 individuals

Hepatitis B Vaccine – Continued

who had received vaccine manufactured from plasma pools that contained plasma of homosexual men. Previous workers have reported that sera of HB vaccine recipients did not show helper-T/supressor-T ratio inversion, a finding common in AIDS patients (*5*).

Epidemiologic approaches to detect an association between HB vaccine and AIDS have included analysis of data on AIDS cases reported to CDC concerning their receipt of HB vaccine and monitoring rates of AIDS in groups of homosexually active men who did or did not receive HB vaccine in the vaccine trials conducted by CDC in Denver, Colorado, and San Francisco, California. To date, 68 AIDS cases have been reported among approximately 700,000 U.S. HB vaccine recipients; 65 have occurred among persons with known AIDS risk factors, while risk factors for the remaining three are under investigation. In addition, the rate of AIDS for HB vaccine recipients in CDC vaccine trials among homosexually active men in Denver and San Francisco does not differ from that for men screened for possible participation in the trials but who received no HB vaccine because they were found immune to HB.

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Editorial Note: The Immunization Practices Advisory Committee (ACIP) (*6*) has recommended preexposure HB vaccination for susceptible members of the following groups in the United States: health-care workers (medical, dental, laboratory, and support groups) judged to have significant exposure to blood or blood products; clients and selected staff of institutions for the mentally retarded; hemodialysis patients; homosexually active males; users of illicit, injectable drugs; recipients of certain blood products (patients with clotting factor disorders); and household and sexual contacts of HB virus (HBV) carriers. In addition, vaccine may be warranted for classroom contacts of deinstitutionalized mentally retarded HBV carriers; special high-risk populations (Alaskan Eskimos and immigrants and refugees from areas with highly endemic disease); inmates of long-term correctional facilities; and some U.S. citizens living or traveling abroad (*7*). The ACIP has also recommended screening all pregnant women belonging to high-risk groups for HB and treating their newborn infants with hepatitis B immune globulin and HB vaccine (*8*).

HB vaccine acceptance in the United States has been seriously hindered by the fear of possible AIDS transmission from the vaccine. The recent identification of AIDS' etiologic agent has made possible direct laboratory measurement of virus inactivation, nucleic acid presence, and serologic evidence of infection. These studies were unable to detect the AIDS virus' viral protein or nucleic acid in the purified vaccine product and clearly indicate that if virus were present, it would be killed by the manufacturing procedures. In addition, epidemiologic monitoring of AIDS cases and high-risk groups confirms the lack of AIDS transmission by HB vaccine. This information should remove a major impediment to vaccine use.

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Hepatitis B Vaccine — Continued

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Acute Convulsions Associated with Endrin Poisoning — Pakistan

Between July 14, and September 26, 1984, an outbreak of acute convulsions occurred in Talagang, a wheat-growing subdistrict of the Punjab province of Pakistan. At least one case was reported in 21 (32%) of 65 villages in the subdistrict. Altogether, 192 cases, with 19 deaths, were reported. Sixty percent of the cases occurred among persons between 1 year and 9 years of age, and 80% occurred among persons under 15 years of age. Males and females were equally affected. None of the patients interviewed had a prior history of seizures.

Young children had no prodromal symptoms before the onset of seizures. They were observed to be engaged in routine activities when they collapsed suddenly, with bilateral jerking of the upper extremities followed by generalized tonic, clonic contractions and frothing or vomiting. Older patients reported having headaches and/or nausea and minor muscular spasms approximately half an hour before collapsing. Among untreated patients, seizures continued intermittently for 15 minutes to more than 2 hours. Repeated attacks were associated with hypoxia, pulmonary congestion, and death. Axillary temperatures of 37.8 C (100 F) were recorded in some patients immediately after the seizures ceased. More severely ill patients did not vomit as frequently as mildly affected patients, and they had higher temperatures. The combination of diazepam, phenobarbital, and atropine (to control secretions) was an effective therapeutic regimen in controlling symptoms. More severely affected patients were also given general anesthesia. For most patients, seizures were controlled within 1-2 hours, and patients remained sleepy for 24-48 hours, then recovered completely. Afterwards, patients did not remember the seizures.

Sera from 12 of 21 patients with convulsions had measurable levels of endrin. Values for all 21 ranged from 0 parts per billion (ppb) to 254 ppb (mean 17.10 ppb; median 1 ppb). Stomach contents from one of the 12 patients whose sera were positive had 307 ppb endrin. Autopsy tissues from another person contained endrin levels consistent with fatal acute exposures. Food samples collected from case homes were negative for endrin. Although 2,4-dichlorophenoxyacetic acid (DDT) and benzene hexachloride (BHC) were found in the homes of many Talagang residents, there was no evidence that endrin was being used by local farmers, nor was it available in the local market.

A case-control study (25 cases, 21 and 23 from two sets of controls) did not implicate causative food or environmental factors. Nevertheless, available data suggested that a common food product (sugar) could have been contaminated during transport to a wholesale depot in the subdistrict capital—the only commercial food distribution point in Talagang—then distributed to the villages. Cases clustered in villages located near the main road to the subdistrict capital. There was little to no communication between villages, but shopkeepers and village residents frequently traveled to the subdistrict capital to purchase supplies. Cotton and sugar-cane growers in the southern part of the Punjab use endrin. Several independent truckers reported delivering chemicals to these growers, then picking up loads of food in the same trucks for transport to Talagang. However, there were no records with which to verify these reports. Additional environmental and food samples from patients' homes and the wholesale food depots are still being analyzed, and results may clarify the source and route of exposure.

Endrin Poisoning — Continued

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Editorial Note: Endrin is a chlorinated hydrocarbon pesticide, one of the group that includes DDT, BHC, chlordane, heptachlor, dieldrin, and aldrin. Endrin, chlordane, heptachlor, dieldrin, and aldrin are structurally similar. All have a cyclodien ring, but endrin is the most toxic. The minimum dose needed to produce a single convulsion in humans and the dose necessary for repeated nonfatal convulsions have been estimated to be 0.2-0.25 mg/kg and 1 mg/kg, respectively (*1*). Endrin is no longer commercially available in the United States. In Pakistan, it is imported for use in the early growth stages of cotton and sugar cane.

Animal studies have found that endrin is rapidly absorbed, metabolized, and excreted in feces, with a half-life in rats ranging from 2 to 6 days. In contrast, dieldrin is redistributed in body organs, particularly fat (*2*). Endrin is not persistent in animals or humans. Unlike DDT, BHC, dieldrin, and some of the other chlorinated hydrocarbons, endrin has not been found in fat samples taken from general surveys of humans exposed to chlorinated hydrocarbons, including endrin (*4*), nor has it been found in the blood of endrin workers, except in association with recent gross accidental exposure (*1,3*). Previously reported blood levels of patients poisoned by ingestion of endrin have ranged from 4 ppb to 53 ppb within the first day of

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TABLE I. Summary—cases of specified notifiable diseases, United States

Disease	49th Week Ending			Cumulative, 49th Week Ending		
	Dec. 8, 1984	Dec. 10, 1983	Median 1979-1983	Dec. 8, 1984	Dec. 10, 1983	Median 1979-1983
Acquired Immunodeficiency Syndrome (AIDS)*	113	98	N	4,072	1,963	N
Aseptic meningitis	140	180	180	7,719	11,958	9,108
Encephalitis: Primary (arthropod-borne & unspec.)	25	24	24	1,108	1,759	1,454
Post-infectious	-	4	2	81	87	87
Gonorrhea: Civilian	16,973	19,145	19,481	786,699	850,539	943,590
Military	372	481	579	19,322	22,726	25,275
Hepatitis: Type A	444	511	601	20,188	20,143	23,985
Type B	552	545	504	24,374	22,559	19,635
Non A, Non B	69	84	N	3,513	3,226	N
Unspecified	109	144	222	5,115	6,830	9,883
Legionellosis	9	16	N	613	715	N
Leprosy	6	5	5	222	226	207
Malaria	27	19	19	935	760	1,002
Measles: Total**	13	8	45	2,511	1,431	2,904
Indigenous	13	7	N	2,219	1,129	N
Imported	-	1	N	292	303	N
Meningococcal infections: Total	58	56	52	2,520	2,564	2,564
Civilian	58	56	52	2,515	2,549	2,549
Military	-	-	-	5	15	15
Mumps	56	54	133	2,738	3,098	5,077
Pertussis	24	29	29	2,066	2,203	1,584
Rubella (German measles)	8	12	42	722	926	2,230
Syphilis (Primary & Secondary): Civilian	538	600	600	25,925	30,388	29,271
Military	2	4	10	271	367	355
Toxic Shock syndrome	11	8	N	438	402	N
Tuberculosis	526	487	529	20,147	22,082	25,447
Tularemia	1	12	4	279	285	244
Typhoid fever	11	10	10	350	438	482
Typhus fever, tick-borne (RMSF)	6	5	4	856	1,092	1,092
Rabies, animal	62	68	93	5,038	5,670	5,930

TABLE II. Notifiable diseases of low frequency, United States

	Cum. 1984		Cum. 1984
Anthrax	1	Plague	30
Botulism: Foodborne	19	Poliomyelitis: Total	4
Infant	89	Paralytic (Calif. 1)	4
Other	6	Psittacosis (N.C. 1, Calif. 1)	85
Brucellosis (Iowa 1, Calif. 2)	118	Rabies, human	3
Cholera	-	Tetanus (Ala. 1)	64
Congenital rubella syndrome	4	Trichinosis	61
Diphtheria	2	Typhus fever, flea-borne (endemic, murine)	35
Leptospirosis	30		

*The 1983 reports which appear in this table were collected before AIDS became a notifiable condition.

**There were no cases of internationally imported measles reported for this week.

TABLE III. Cases of specified notifiable diseases, United States, weeks ending December 8, 1984 and December 10, 1983 (49th Week)

Reporting Area	AIDS	Aseptic Meningitis	Encephalitis		Gonorrhea (Civilian)		Hepatitis (Viral), by type				Legionellosis	Leprosy
			Primary	Post-infectious			A	B	NA,NB	Unspecified		
	Cum. 1984	1984	Cum. 1984	Cum. 1984	Cum. 1984	Cum. 1983	1984	1984	1984	1984	1984	Cum. 1984
UNITED STATES	4,072	140	1,108	81	786,699	850,539	444	552	69	109	9	222
NEW ENGLAND	137	1	47	2	21,731	22,414	4	41	-	5	-	11
Maine	-	-	-	-	959	1,085	-	-	-	-	-	-
N.H.	2	-	7	-	686	694	-	2	-	-	-	-
Vt.	1	-	5	-	364	414	-	2	-	-	-	-
Mass.	74	1	21	-	9,222	9,768	3	32	-	5	-	6
R.I.	6	-	-	-	1,549	1,223	-	-	-	-	-	4
Conn.	54	-	14	2	8,951	9,250	1	5	-	-	-	1
MID ATLANTIC	1,776	13	121	9	106,637	110,224	35	72	4	4	1	36
Upstate N.Y.	153	4	40	7	17,284	17,911	5	5	1	1	-	3
N.Y. City	1,301	1	11	-	41,202	44,248	11	31	-	1	-	31
N.J.	233	3	28	-	19,050	20,464	5	17	-	1	1	-
Pa.	89	5	42	2	29,101	27,601	14	19	3	1	-	2
E.N. CENTRAL	181	35	324	18	113,619	122,618	25	67	5	6	1	6
Ohio	20	13	102	9	29,282	31,773	11	22	1	2	1	2
Ind.	24	2	82	-	12,149	11,763	1	8	2	3	-	-
Ill.	97	7	37	6	26,911	35,404	-	-	-	-	-	2
Mich.	30	13	67	-	32,768	32,728	11	37	2	1	-	2
Wis.	10	-	36	3	12,509	10,950	2	-	-	-	-	-
W.N. CENTRAL	39	4	98	3	39,313	40,021	11	18	3	1	-	4
Minn.	9	-	46	-	5,880	5,639	-	-	-	-	-	2
Iowa	2	2	31	-	4,307	4,365	2	1	-	-	-	1
Mo.	23	1	11	-	18,856	19,497	1	9	2	-	-	1
N. Dak.	-	-	-	-	380	421	-	-	-	-	-	-
S. Dak.	-	-	2	1	944	994	7	-	1	-	-	-
Nebr.	3	-	1	-	2,855	2,626	-	5	-	-	-	-
Kans.	2	1	7	2	6,091	6,479	1	3	-	1	-	-
S. ATLANTIC	532	27	169	17	192,246	220,030	25	91	12	9	1	14
Del.	5	-	1	-	3,846	4,062	1	-	1	-	-	-
Md.	46	2	33	-	22,790	28,360	2	4	-	-	-	1
D.C.	81	1	-	-	14,352	14,974	1	1	-	-	-	1
Va.	38	4	29	5	19,128	20,101	3	13	2	2	-	4
W. Va.	5	1	40	-	2,549	2,490	-	2	-	-	-	-
N.C.	14	3	32	7	32,456	33,838	1	3	1	1	-	-
S.C.	8	5	5	-	20,537	20,282	1	16	1	2	-	-
Ga.	55	1	2	2	28,722	46,293	4	15	1	-	1	1
Fla.	280	10	27	3	47,866	49,630	12	37	6	4	-	7
E.S. CENTRAL	24	4	51	8	71,810	71,528	4	36	3	1	-	-
Ky.	10	-	13	-	8,509	8,474	1	7	-	1	-	-
Tenn.	6	1	16	1	28,923	29,298	-	10	1	-	-	-
Ala.	6	-	19	6	21,575	22,019	1	14	2	-	-	-
Miss.	2	3	3	1	12,803	11,737	2	5	-	-	-	-
W.S. CENTRAL	288	22	105	4	107,144	118,367	104	38	6	50	4	24
Ark.	1	-	-	2	9,503	9,463	9	4	1	-	-	1
La.	43	2	12	-	23,309	22,850	3	4	-	3	-	1
Okla.	9	2	19	1	11,817	13,636	26	-	1	3	1	-
Tex.	235	18	74	1	62,515	72,418	66	30	4	44	3	22
MOUNTAIN	70	7	34	11	26,192	27,048	44	44	3	10	-	8
Mont.	-	1	-	-	971	1,148	-	-	-	-	-	-
Idaho	-	1	-	-	1,207	1,210	-	-	-	-	-	-
Wyo.	1	-	-	-	700	717	2	-	1	-	-	-
Colo.	36	3	12	-	7,466	7,531	12	6	-	5	-	-
N. Mex.	2	-	-	-	3,128	3,332	4	4	-	-	-	-
Ariz.	18	-	12	3	7,472	7,720	17	23	2	5	-	6
Utah	7	2	10	8	1,229	1,295	2	3	-	-	-	1
Nev.	6	-	-	-	4,019	4,095	7	8	-	-	-	1
PACIFIC	1,025	27	159	9	108,007	118,289	192	145	33	23	2	119
Wash.	52	8	9	-	8,332	9,292	19	11	2	1	-	8
Oreg.	14	-	-	-	6,271	6,318	26	14	7	-	-	1
Calif.	945	19	147	9	88,812	97,456	147	120	24	22	2	91
Alaska	2	-	-	-	2,729	3,014	-	-	-	-	-	-
Hawaii	12	-	3	-	1,863	2,209	-	-	-	-	-	19
Guam	-	U	-	-	103	129	U	U	U	U	U	
P.R.	63	7	3	2	3,166	2,615	6	9	-	8	-	5
V.I.	-	-	-	-	427	304	-	-	-	-	-	-
Pac. Trust Terr.	-	U	-	-	-	-	U	U	U	U	U	-

N: Not notifiable U: Unavailable

TABLE III. (Cont'd.) Cases of specified notifiable diseases, United States, weeks ending December 8, 1984 and December 10, 1983 (49th Week)

Reporting Area	Malaria	Measles (Rubeola)					Menin-gococcal infections	Mumps		Pertussis			Rubella		
		Indigenous		Imported *		Total									
	Cum. 1984	1984	Cum. 1984	1984	Cum. 1984	Cum. 1983	Cum. 1984	1984	Cum. 1984	1984	Cum. 1984	Cum. 1983	1984	Cum. 1984	Cum. 1983
UNITED STATES	935	13	2,219	-	292	1,431	2,520	56	2,738	24	2,066	2,203	8	722	926
NEW ENGLAND	47	-	94	-	12	21	173	2	93	1	68	73	-	21	19
Maine	-	-	-	-	-	-	1	-	29	-	4	5	-	1	-
N.H.	-	-	33	-	3	3	11	1	19	-	14	10	-	1	5
Vt.	7	-	2	-	8	-	29	-	5	-	23	8	-	-	5
Mass.	26	-	49	-	-	9	70	-	20	1	19	38	-	18	7
R.I.	4	-	-	-	-	-	18	1	11	-	4	5	-	-	-
Conn.	10	-	10	-	4	9	44	-	9	-	4	7	-	1	2
MID ATLANTIC	143	4	135	-	44	119	436	3	313	4	195	375	1	229	145
Upstate N.Y.	28	4	42	-	14	18	139	2	96	4	108	117	-	99	30
N.Y. City	48	-	89	-	20	71	87	-	30	-	16	56	1	104	86
N.J.	37	-	4	-	3	27	86	1	136	-	13	20	-	22	3
Pa.	30	-	-	-	7	3	124	-	49	-	58	182	-	4	26
E.N. CENTRAL	82	-	617	-	75	712	406	25	1,055	10	460	495	-	96	136
Ohio	19	-	3	-	6	87	133	5	493	-	76	150	-	2	2
Ind.	4	-	2	-	1	406	51	11	74	10	241	58	-	5	26
Ill.	28	-	179	-	1	211	87	7	186	-	26	172	-	59	60
Mich.	17	-	411	-	54	7	84	2	187	-	31	42	-	22	19
Wis.	14	-	22	-	13	1	51	-	115	-	86	73	-	8	29
W.N. CENTRAL	24	-	49	-	9	8	159	1	108	1	126	139	-	39	42
Minn.	7	-	44	-	3	1	35	-	7	-	16	47	-	4	9
Iowa	2	-	-	-	-	-	23	-	25	1	14	9	-	1	-
Mo.	8	-	5	-	1	1	49	-	10	-	20	23	-	-	-
N. Dak.	1	-	-	-	-	-	2	-	2	-	-	3	-	3	-
S. Dak.	1	-	-	-	-	-	6	-	-	-	9	8	-	-	-
Nebr.	3	-	-	-	-	-	13	-	4	-	13	4	-	-	-
Kans.	2	-	-	-	5	6	31	1	60	-	54	45	-	31	33
S. ATLANTIC	124	-	19	-	33	206	516	3	196	4	168	261	2	29	99
Del.	4	-	-	-	-	-	4	1	3	-	2	5	-	2	-
Md.	30	-	8	-	14	11	39	1	41	-	13	34	-	1	3
D.C.	1	-	-	-	5	-	8	-	-	-	-	-	-	-	-
Va.	34	-	1	-	4	23	64	-	18	-	15	50	-	1	2
W. Va.	1	-	-	-	-	-	5	-	39	-	11	9	-	-	-
N.C.	12	-	-	-	1	1	85	1	22	1	36	29	-	-	10
S.C.	2	-	-	-	-	4	57	-	5	-	1	14	-	-	1
Ga.	14	-	1	-	1	8	99	-	22	1	18	69	-	2	13
Fla.	26	-	9	-	8	159	155	-	48	2	72	51	2	23	70
E.S. CENTRAL	11	-	1	-	5	25	139	1	55	-	14	33	-	20	19
Ky.	2	-	1	-	-	1	50	-	11	-	2	14	-	14	18
Tenn.	2	-	-	-	2	-	38	-	17	-	7	8	-	-	-
Ala.	7	-	-	-	3	5	34	-	6	-	1	5	-	3	1
Miss.	-	-	-	-	-	19	17	1	21	-	4	6	-	3	-
W.S. CENTRAL	84	-	596	-	25	79	285	8	179	2	328	449	2	68	120
Ark.	-	-	8	-	-	13	46	-	8	-	19	26	-	3	-
La.	9	-	8	-	-	29	57	-	-	-	10	11	-	-	10
Okla.	10	-	-	-	8	1	28	N	N	2	240	330	-	-	-
Tex.	65	-	580	-	17	36	154	8	171	-	59	82	2	65	110
MOUNTAIN	27	-	113	-	32	31	83	5	258	-	122	230	-	22	36
Mont.	2	-	-	-	-	4	2	1	10	-	19	2	-	-	3
Idaho	2	-	-	-	23	10	10	-	10	-	7	16	-	1	8
Wyo.	-	-	-	-	-	1	3	-	2	-	6	6	-	3	8
Colo.	7	-	-	-	6	3	28	-	28	-	45	133	-	2	1
N. Mex.	1	-	88	-	-	-	8	N	N	-	12	13	-	1	-
Ariz.	10	-	-	-	1	1	17	3	191	-	24	29	-	4	8
Utah	5	-	25	-	2	12	9	-	11	-	7	31	-	7	7
Nev.	-	-	-	-	-	-	6	1	6	-	2	-	-	4	1
PACIFIC	393	9	595	-	57	230	323	8	479	2	585	148	3	198	310
Wash.	20	6	144	-	15	35	51	-	52	1	321	20	1	2	9
Oreg.	14	-	-	-	-	10	47	N	N	-	30	10	-	2	14
Calif.	354	3	292	-	38	181	216	7	389	-	157	111	2	187	285
Alaska	-	-	-	-	-	2	8	1	14	-	1	4	-	1	1
Hawaii	5	-	159	-	4	2	1	-	24	1	76	3	-	6	1
Guam	1	U	83	U	2	2	1	U	5	U	-	-	U	2	-
P.R.	4	14	210	-	-	96	6	1	172	-	1	14	-	20	8
V.I.	-	-	-	-	-	5	-	-	5	-	-	-	-	-	2
Pac. Trust Terr.	-	U	-	U	-	-	-	U	-	U	-	-	U	-	-

*For measles only, imported cases includes both out-of-state and international importations.

N: Not notifiable U: Unavailable †International §Out-of-state

TABLE III. (Cont'd.) Cases of specified notifiable diseases, United States, weeks ending December 8, 1984 and December 10, 1983 (49th Week)

Reporting Area	Syphilis (Civilian) (Primary & Secondary)		Toxic-shock Syndrome	Tuberculosis		Tula-remia	Typhoid Fever	Typhus Fever (Tick-borne) (RMSF)	Rabies, Animal
	Cum. 1984	Cum. 1983	1984	Cum. 1984	Cum. 1983	Cum. 1984	Cum. 1984	Cum. 1984	Cum. 1984
UNITED STATES	25,925	30,588	11	20,147	22,062	279	350	856	5,038
NEW ENGLAND	501	647	-	603	672	7	20	6	47
Maine	10	19	-	33	35	-	-	-	13
N.H.	14	22	-	27	35	-	-	-	16
Vt.	1	3	-	8	11	-	-	-	-
Mass.	281	418	-	328	357	7	17	4	10
R.I.	22	23	-	48	62	-	-	-	-
Conn.	173	162	-	159	172	-	3	2	8
MID ATLANTIC	3,478	4,030	1	3,693	3,934	2	54	27	525
Upstate N.Y.	271	376	-	571	615	-	12	10	120
N.Y. City	2,099	2,326	-	1,532	1,583	2	18	3	-
N.J.	625	785	1	798	811	-	18	3	37
Pa.	483	543	-	792	925	-	6	11	368
E.N. CENTRAL	1,323	1,618	4	2,621	2,965	9	56	64	208
Ohio	226	431	1	467	471	1	7	39	25
Ind.	140	139	-	329	329	-	11	7	21
Ill.	538	731	-	1,087	1,281	8	22	15	74
Mich.	347	229	3	589	735	-	7	3	21
Wis.	72	88	-	149	149	-	9	-	67
W.N. CENTRAL	339	368	-	602	708	83	10	54	739
Minn.	87	141	-	108	148	1	3	1	94
Iowa	11	23	-	62	65	-	-	6	143
Mo.	173	137	-	298	353	45	5	19	66
N. Dak.	9	2	-	13	6	-	-	-	140
S. Dak.	1	11	-	22	37	34	-	5	203
Nebr.	15	15	-	30	25	-	-	5	44
Kans.	43	39	-	69	74	3	2	18	49
S. ATLANTIC	7,378	8,243	2	4,249	4,386	8	40	394	1,496
Del.	20	35	-	56	64	-	-	1	6
Md.	458	495	-	422	347	1	2	28	846
D.C.	316	364	-	169	180	1	6	-	-
Va.	395	537	-	436	485	1	8	50	200
W. Va.	20	25	-	126	127	-	-	7	40
N.C.	815	827	-	635	699	1	1	176	25
S.C.	735	543	-	505	422	-	1	79	59
Ga.	1,059	1,473	-	654	715	4	8	48	181
Fla.	3,560	3,944	2	1,246	1,347	-	14	5	139
E.S. CENTRAL	1,907	2,042	-	1,879	1,979	7	9	94	245
Ky.	94	168	-	436	492	1	2	19	52
Tenn.	494	541	-	548	605	5	2	49	78
Ala.	636	786	-	549	496	-	2	15	115
Miss.	683	547	-	346	386	1	3	11	-
W.S. CENTRAL	6,409	7,746	1	2,366	2,743	117	24	200	971
Ark.	189	182	-	266	338	83	-	28	100
La.	1,129	1,578	-	337	421	7	2	4	57
Okla.	203	189	1	223	254	19	4	118	99
Tex.	4,888	5,797	-	1,540	1,730	8	18	50	715
MOUNTAIN	636	627	-	540	617	33	13	13	276
Mont.	3	7	-	17	42	3	1	8	123
Idaho	23	7	-	28	30	8	-	1	11
Wyo.	4	12	-	4	12	1	-	3	25
Colo.	171	144	-	66	92	6	5	1	39
N. Mex.	91	172	-	103	108	2	3	-	11
Ariz.	232	160	-	251	247	4	3	-	45
Utah	18	22	-	34	40	4	-	-	6
Nev.	94	103	-	37	46	5	1	-	16
PACIFIC	3,954	5,067	3	3,594	4,058	13	124	4	531
Wash.	133	190	1	189	224	3	3	-	3
Oreg.	112	139	-	142	171	2	2	1	1
Calif.	3,628	4,649	2	2,982	3,363	8	110	2	519
Alaska	6	13	-	75	73	-	1	1	8
Hawaii	75	76	-	206	227	-	8	-	-
Guam	-	-	U	5	9	-	-	-	-
P.R.	749	879	-	380	447	-	5	-	61
V.I.	11	19	-	3	2	-	3	-	-
Pac. Trust Terr.	-	-	U	-	-	-	-	-	-

U: Unavailable

TABLE IV. Deaths in 121 U.S. cities,* week ending December 8, 1984 (49th Week Ending)

Reporting Area	All Causes, By Age (Years)						P&I** Total
	All Ages	≥65	45-64	25-44	1-24	<1	
NEW ENGLAND	618	431	118	33	13	26	40
Boston, Mass.	171	117	25	11	5	13	15
Bridgeport, Conn.	41	26	9	2	3	1	3
Cambridge, Mass.	34	25	7	2	-	-	4
Fall River, Mass.	30	27	3	-	-	-	-
Hartford, Conn.	52	40	8	1	1	2	1
Lowell, Mass.	25	21	-	2	1	1	3
Lynn, Mass.	23	16	5	2	-	-	-
New Bedford, Mass.	20	11	8	1	-	-	-
New Haven, Conn.	50	30	11	3	1	5	2
Providence, R.I.	38	24	9	2	1	2	2
Somerville, Mass.	10	8	2	-	-	-	1
Springfield, Mass.	36	24	10	-	1	1	4
Waterbury, Conn.	27	18	7	2	-	-	2
Worcester, Mass.	61	44	11	5	-	1	3
MID. ATLANTIC	2,740	1,825	581	210	50	74	147
Albany, N.Y.	39	33	4	1	-	1	4
Allentown, Pa.	11	10	1	-	-	-	-
Buffalo, N.Y.	137	94	32	7	2	2	10
Camden, N.J.	51	28	13	5	3	4	3
Elizabeth, N.J.	32	20	11	1	-	-	2
Erie, Pa.†	64	53	10	-	-	1	6
Jersey City, N.J.	40	25	11	4	-	-	2
N.Y. City, N.Y.	1,540	1,013	317	136	30	44	75
Newark, N.J.	72	42	17	4	2	7	1
Paterson, N.J.	27	14	8	3	1	1	-
Philadelphia, Pa.†	250	162	54	23	7	4	11
Pittsburgh, Pa.†	66	38	20	4	-	4	2
Reading, Pa.	31	22	4	5	-	-	7
Rochester, N.Y.	107	84	14	3	2	4	10
Schenectady, N.Y.	30	19	9	2	-	-	4
Scranton, Pa.†	36	28	8	-	-	-	1
Syracuse, N.Y.	110	75	24	6	3	2	3
Trenton, N.J.	48	31	13	4	-	-	2
Utica, N.Y.	22	16	5	1	-	-	1
Yonkers, N.Y.	27	20	6	1	-	-	3
E.N. CENTRAL	2,242	1,600	418	94	55	65	85
Akron, Ohio	79	65	10	1	2	1	1
Canton, Ohio	50	35	12	2	-	1	8
Chicago, Ill. §	459	413	5	8	11	13	11
Cincinnati, Ohio	121	80	32	5	1	3	9
Cleveland, Ohio	152	90	49	8	1	4	2
Columbus, Ohio	135	87	28	9	7	4	1
Dayton, Ohio	111	77	25	5	1	3	5
Detroit, Mich.	271	176	59	14	7	14	5
Evansville, Ind.	34	22	8	1	2	1	-
Fort Wayne, Ind.	47	32	9	3	1	2	1
Gary, Ind.	12	4	6	2	-	-	1
Grand Rapids, Mich.	70	56	9	2	3	-	2
Indianapolis, Ind.	211	127	53	16	6	9	4
Madison, Wis.	25	20	3	-	1	1	2
Milwaukee, Wis.	121	90	27	3	1	-	10
Peoria, Ill.	86	48	26	3	3	6	8
Rockford, Ill.	50	33	10	5	2	-	2
South Bend, Ind.	46	32	10	1	1	2	4
Toledo, Ohio	103	71	22	4	5	1	7
Youngstown, Ohio	59	42	15	2	-	-	2
W.N. CENTRAL	882	632	153	47	13	37	56
Des Moines, Iowa	65	47	12	3	1	2	6
Duluth, Minn.	22	18	3	-	-	1	1
Kansas City, Kans.	35	22	6	5	1	1	1
Kansas City, Mo.	151	113	21	10	1	6	8
Lincoln, Nebr.	47	29	9	5	2	2	3
Minneapolis, Minn.	90	56	19	7	2	6	9
Omaha, Nebr.	113	78	27	2	1	5	11
St. Louis, Mo.	148	109	21	8	1	9	5
St. Paul, Minn.	97	76	14	4	2	1	1
Wichita, Kans.	114	84	21	3	2	4	11
S. ATLANTIC	1,634	945	372	175	62	79	69
Atlanta, Ga.	208	131	51	17	3	6	4
Baltimore, Md.	206	132	50	13	3	8	6
Charlotte, N.C.	94	51	25	11	2	5	3
Jacksonville, Fla.	111	71	25	4	8	3	13
Miami, Fla.	121	68	27	16	5	5	-
Norfolk, Va.	47	27	9	2	4	5	7
Richmond, Va.	82	43	22	11	4	2	6
Savannah, Ga.	64	37	13	1	1	12	6
St. Petersburg, Fla.	126	107	15	4	-	-	11
Tampa, Fla.	79	43	19	11	3	2	5
Washington, D.C.	459	213	108	84	27	27	8
Wilmington, Del.	37	22	8	1	2	4	-
E.S. CENTRAL	798	478	229	46	20	25	40
Birmingham, Ala.	124	63	47	6	4	4	3
Chattanooga, Tenn.	46	30	13	2	-	1	5
Knoxville, Tenn.	92	61	21	2	5	3	5
Louisville, Ky.	128	80	36	7	2	3	9
Memphis, Tenn.	174	106	49	11	2	6	12
Mobile, Ala.	67	41	16	4	2	4	2
Montgomery, Ala.	45	25	12	4	2	2	1
Nashville, Tenn.	122	72	35	10	3	2	3
W.S. CENTRAL	1,369	792	335	117	62	63	56
Austin, Tex.	63	35	16	4	6	-	4
Baton Rouge, La.	38	21	9	2	4	2	2
Corpus Christi, Tex.	29	22	3	1	1	2	1
Dallas, Tex.	239	126	58	28	12	15	7
El Paso, Tex.	60	40	13	2	3	2	5
Fort Worth, Tex.	100	67	19	8	3	3	10
Houston, Tex.	309	155	87	40	15	12	4
Little Rock, Ark.	62	32	21	6	2	1	6
New Orleans, La.	150	85	35	12	3	15	4
San Antonio, Tex.	204	124	53	11	8	8	9
Shreveport, La.	33	26	3	2	1	1	-
Tulsa, Okla.	82	59	18	1	2	2	4
MOUNTAIN	708	454	154	39	23	38	31
Albuquerque, N.Mex.	92	57	23	5	5	2	3
Colo. Springs, Colo.	36	25	6	2	1	2	3
Denver, Colo.	129	81	20	7	4	17	10
Las Vegas, Nev.	92	59	21	5	3	4	2
Ogden, Utah	13	9	2	-	1	1	2
Phoenix, Ariz.	174	108	41	12	7	6	2
Pueblo, Colo.	25	19	5	-	-	1	1
Salt Lake City, Utah	47	30	9	4	1	3	-
Tucson, Ariz.	100	66	27	4	1	2	8
PACIFIC	1,804	1,320	281	104	46	40	91
Berkeley, Calif.	19	17	1	1	-	-	-
Fresno, Calif.	76	46	17	8	3	2	4
Glendale, Calif.§	18	18	-	-	-	-	-
Honolulu, Hawaii	75	56	11	5	3	-	3
Long Beach, Calif.	98	64	24	5	3	-	-
Los Angeles, Calif. §	402	366	4	1	15	5	9
Oakland, Calif.	70	45	9	11	2	3	3
Pasadena, Calif.	25	19	3	1	1	1	3
Portland, Oreg.	110	74	24	7	3	2	4
Sacramento, Calif.	138	101	25	5	3	3	11
San Diego, Calif.	171	105	44	14	2	6	18
San Francisco, Calif.	172	110	36	22	1	3	3
San Jose, Calif.	176	123	31	13	3	5	20
Seattle, Wash.	181	106	39	7	4	5	2
Spokane, Wash.	51	36	10	3	-	2	8
Tacoma, Wash.	44	34	3	1	3	3	3
TOTAL	12,795††	8,477	2,638	885	344	447	615

* Mortality data in this table are voluntarily reported from 121 cities in the United States, most of which have populations of 100,000 or more. A death is reported by the place of its occurrence and by the week that the death certificate was filed. Fetal deaths are not included.

** Pneumonia and influenza.

† Because of changes in reporting methods in these 4 Pennsylvania cities, these numbers are partial counts for the current week. Complete counts will be available in 4 to 6 weeks.

†† Total includes unknown ages.

§ Data not available. Figures are estimates based on average of past 4 weeks.

Endrin Poisoning — Continued

consuming contaminated food (*5,6*). No endrin was detected 29-31 days after exposure (*6*). The presence of endrin in 57% of seizure patients tested in Pakistan suggests that endrin was the cause of this most recent outbreak.

Previous outbreaks of endrin poisoning have been associated with consumption of contaminated flour. Bread and rolls from the outbreaks contained 126-180 parts per million of endrin (*5,7*). The first reported outbreak was in Great Britain, where endrin was spilled on the floor of a box car; 1 month later, bags of flour stacked on the floor of the car became contaminated (*8*). In the Middle East, over 800 cases of endrin poisoning occurred in four outbreaks after contaminated flour was used in several bakeries (*7*). The flour had been imported aboard ships that were also transporting endrin. Endrin spilled from the upper decks of the ships onto the sacks of flour. As a result of the investigation, the governments of Qatar and Saudi Arabia required that ships transporting foodstuffs identify the type and location of all toxic chemicals and that the ships be inspected before food was unloaded for delivery (*7*).

In the Pakistan episode, circumstances of endrin use and food and chemical transport suggest that food products could have been contaminated during transport. Whether further analysis of environmental samples and epidemiologic data can document the source(s) and route(s) of exposure remains to be seen.

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Human *Salmonella* Isolates — United States, 1983

In 1983, 38,881 *Salmonella* isolates (including *Salmonella typhi*) from humans were reported to CDC. This represents a 3.2% increase over the 37,683 isolates reported in 1982. During the past 16 years, the number of *Salmonella* isolates reported to CDC has continued to rise from the 19,659 isolates reported in 1968. The increase was not confined to one state or region. Notable increases over 1982 were seen in: Maryland—183% increase (442 to 1,251); Vermont—119% increase (73 to 160); Indiana—105% increase (242 to 497); New Mexico—37% increase (243 to 333); Utah—34% increase (85 to 114); Oklahoma—33% increase (272 to 361); Alabama—31% increase (561 to 743); and New York—27% increase (2,300 to 2,916). The extent to which these increases represent reporting artifacts is unknown.

The 10 most frequently reported isolates comprised 71% of all the isolates reported (Table 1). *S. heidelberg* increased 42% (2,641 isolates in 1982 to 3,746 isolates in 1983), and *S. agona* increased 24% (1,125 to 1,396).

Increases were also reported in some less frequently isolated serotypes. *S. stanleyville* increased from one isolate reported in 1982 to 37 in 1983; 57% of these isolates were report-

Human Salmonella — *Continued*

ed by New York state. *S. djuju* increased from three reported isolates to 24; an outbreak at a catered party in Alabama was partially responsible for this increase. *S. tennessee* increased from 59 to 136 reported isolates; increases were reported by Illinois and Virginia. *S. braenderup* increased from 212 to 324; an outbreak of this serotype was reported in a restaurant in Illinois. Reported isolates of *S. havana* increased from 71 to 114; an outbreak that occurred in a North Carolina hospital was in part responsible for this increase. *S. dublin* increased from 126 to 182; 66% of these isolates were reported by California. *S. hadar* increased from 144 to 325; 40% of these isolates were reported by New Jersey, New York, North Carolina, and Virginia.

Age data were reported for 80% of the isolates. The reported rates of *Salmonella* isolation were highest for 2- to 4-month-old infants, decreased abruptly among early childhood age groups, and then remained relatively constant through the adult years. The reported rates were slightly higher among males in the under-20-year age groups and slightly higher among females in the 20- to 69-year age groups. This is consistent with reports from previous years. During the past 16 years, the median age of all persons from whom isolates were obtained has increased from a median of 6 years in 1968 to 14 years in 1982 and 1983.

In 1983, 525 *S. typhi* isolates were reported: 156 were from cases; 26 were from carriers; and the remaining were not designated as to case or carrier status. The carriers' median age was 61; the median age of cases was 25.

Reported by Statistical Svcs Activity, Enteric Diseases Br, Div of Bacterial Diseases, Center for Infectious Diseases, CDC.

Editorial Note: This report is based on the *Salmonella* surveillance activity conducted by the Association of State and Territorial Epidemiologists, the Association of State and Territorial Public Health Laboratory Directors, and CDC. It is a passive laboratory-based system that receives weekly reports from the states and the District of Columbia and regular summaries from the U.S. Department of Agriculture. The reports do not distinguish between clinical and subclinical infections or between chronic and convalescent carriers. Many factors affect whether an infection will be reported; however, these data permit comparison with past and future tabulations and have provided information for epidemiologic investigations and a crude index of the effectiveness of various public health measures.

In many of the detected outbreaks, the cause was a relatively uncommon serotype, which points to the importance of serotyping *Salmonella*. An increase in a common serotype is less likely to be recognized as an outbreak. Recently, however, identification of outbreaks caused by common serotypes has been facilitated by the application of molecular biologic techniques, such as plasmid profile analysis.

Information from epidemiologic investigations during 1983 has added to the understand-

TABLE 1. *Salmonella* serotypes most frequently isolated from humans — United States, 1983

Serotype	No. isolates (%)	Median age of persons from whom isolates were obtained
*S. typhimurium**	13,172 (33.9)	10 yrs.
S. heidelberg	3,746 (9.6)	5 yrs.
S. enteritidis	3,256 (8.4)	24 yrs.
S. newport	2,071 (5.3)	17 yrs.
S. agona	1,396 (3.6)	18 yrs.
S. infantis	1,272 (3.3)	18 yrs.
S. saint paul	711 (1.8)	20 yrs.
S. montevideo	658 (1.7)	20 yrs.
S. oranienburg	578 (1.5)	22 yrs.
S. typhi	525 (1.4)	26 yrs.
Subtotal	27,385 (70.5)	
Total	**38,881**	

*Includes *S. typhimurium* var. Copenhagen.

Human Salmonella — *Continued*

ing of salmonellosis. In early 1983, 18 persons in four midwest states developed salmonellosis. These patients, most of whom had developed severe salmonellosis after taking antimicrobials for other illnesses, were infected with multi-drug-resistant *S. newport*. The investigation demonstrated that this organism was transmitted by hamburger from a beef herd that had been fed subtherapeutic doses of an antimicrobial for growth promotion (*1*). This outbreak demonstrated that antimicrobial-resistant bacteria of animal origin can cause serious human disease, especially among persons taking antimicrobials. A second investigation of *S. dublin* infections in California confirmed the findings of previous studies linking *S. dublin* to the consumption of certified raw milk (CRM) (*2*). The risk of contracting *S. dublin* for California CRM drinkers in 1983 was calculated to be 158 times greater than the California population that did not drink CRM. A third study in Puerto Rico again associated pet turtles with human disease (*3*). This study of salmonellosis among children under 1 year of age showed that turtles were responsible for 12%-17% of reported infant salmonellosis in Puerto Rico. Although the U.S. Food and Drug Administration banned interstate and intrastate commercial distribution of turtles under 4 inches long in 1975, pet turtles raised in and exported from the United States continue to pose a public health problem. These animals remain inappropriate pets for children.

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Diphtheria-Tetanus-Pertussis Vaccine Shortage — United States

In the past 6 months, major changes have occurred in the pattern of manufacture and distribution of diphtheria-tetanus-pertussis* (DTP) vaccine in the United States. Now, two of the three U.S. commercial manufacturers (Wyeth and Connaught, Inc.) have stopped distribution of their products. Thus, only one manufacturer (Lederle) now markets DTP vaccine in the United States. Lederle has been increasing its production and expanding its facilities to meet current needs. Careful monitoring of supplies and production schedules previously indicated that national supplies would be adequate. However, some recent lots of Lederle DTP vaccine have failed to meet the manufacturer's requirements for release. Production and testing of this three-component vaccine is complex and requires several months. No new vaccine lots may be available until sometime in February 1985. Comparison of available stocks and the quantity of DTP vaccine now being distributed with the usual national utilization of DTP vaccine indicates that, if current use patterns continue, beginning in January 1985, supplies of DTP vaccine will be very limited, and some areas may be without DTP vaccine. This situation may continue through most of 1985.

To minimize the health impact of this shortage, two major options exist—to reduce the amount of vaccine given in a particular dose and to postpone one or more doses. Because it is impossible to predict the degree of protection conferred by partial doses, this option is not recommended (*1*). Consequently, consideration has been given to the possibility of postponing one or more doses of the current immunization schedule, which calls for the administration of DTP vaccine at 2, 4, 6, and 18 months of age, with a fifth dose at 4-6 years of age.

With pertussis, there is a significant risk of infection in infancy and early childhood, with 2,463 cases reported in 1983 (51% of them among infants under 1 year old). Additionally, infants are more likely to suffer complications or death from pertussis than are older children. Consequently, it is critical to continue providing protection against pertussis to infants. The

*Diphtheria and Tetanus Toxoids and Pertussis Vaccine, Adsorbed.

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first three doses of DTP vaccine provide protection against pertussis in 70%-90% of recipients and immunity to diphtheria and tetanus in over 90% of recipients (*2-4*). The doses given at 18 months and at 4-6 years of age enhance protection through the preschool and early school years, respectively.

Taking all these factors into account, interim postponement of the doses of DTP vaccine given at 18 months and at 4-6 years of age could achieve substantial savings in the rate of DTP vaccine use, while still protecting those at greatest risk of these diseases. To have enough vaccine to provide initial protection to all young infants until larger quantities of DTP vaccine are again available, it will be necessary to begin this approach immediately.

After consultation with members of the Immunization Practices Advisory Committee and the Committee on Infectious Diseases of the American Academy of Pediatrics, the following interim recommendations are made:

1. Effective immediately, all health-care providers should postpone administration of the DTP vaccine doses usually given at 18 months and 4-6 years of age (fourth and fifth doses) until greater supplies are available.
2. When adequate DTP vaccine becomes available, steps should be taken to recall all children under 7 years of age who miss these doses for remedial immunization.

If these recommendations are followed by all providers of DTP vaccine throughout this temporary vaccine shortage, immunity in infants will be maintained at the best possible levels. Public health-care providers and professional organizations throughout the United States have been notified and are being urged to follow these recommendations.

Reported by U.S. Public Health Service Interagency Group to Monitor Vaccine Development, Production, and Usage.

References

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